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Up in the Air: Does Ground-Level Ozone Trigger Kawasaki Disease?

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Kawasaki disease occurs most often in children of East Asian ancestry,[1] but the known genetic factors[2] cannot explain why more children have been diagnosed with the disease in recent years, according to Bing-Fang Hwang, an environmental epidemiologist at China Medical University in Taiwan. Hwang and colleagues now report an association between exposure to ground-level ozone and increased risk of Kawasaki disease in a group of young Taiwanese children.[3]

Kawasaki disease is a childhood ailment that causes fever, rash, and a red tongue, among other symptoms. It leads to inflammation in blood vessels throughout the child's body. Most children recover from the disease within a few weeks, but up to one-quarter develop heart problems, including coronary artery aneurysms, arrhythmias, and even heart failure.[4]

The incidence of Kawasaki disease in children under age 5 is highest in Japan (264.8 per 100,000 children), followed by Korea (132.4 per 100,000 children) and Taiwan (82.77 per 100,000 children).[5] Although many nations around the world, including Taiwan, have reported an increase in the number of Kawasaki disease diagnoses in the past decade, it is not clear whether these reports represent a true rise in incidence or just greater awareness of the disease.[6]

Despite decades of research, the origins of Kawasaki disease are not fully understood. "It follows an immunological pattern that does not look like any other disease we know," says Jane Burns, director of the Kawasaki Disease Research Center at the University of California, San Diego, School of Medicine, who was not involved with the study. There is evidence that viral infection may play a role,[7] and other previous studies have suggested that some windborne environmental factors may trigger the disease in genetically susceptible children.[8,9]

In the new study, Hwang and colleagues used a Taiwanese health insurance database to identify 695 hospitalizations for Kawasaki disease in children under age 5 between 2000 and 2010. The team then estimated daily levels of five air pollutants near the home of each child, accounting for atmospheric variables including temperature, humidity, and wind direction.

The researchers found an association between hospitalizations for Kawasaki disease and ozone pollution for the summer months only, possibly because children spend more time outdoors in the summertime. When they divided patients into four groups based on their estimated level of ozone exposure, hospitalization was more likely for children in the three highest quartiles compared with the lowest, although the association was not statistically significant for the third quartile of exposure. They also found no significant associations with other pollutants, including nitrogen dioxide and coarse particulate matter.

The study contributes to the growing body of research highlighting the link between Kawasaki disease and the environment, says Xavier Rodó, an atmospheric scientist who studies Kawasaki disease at the Catalan Institute of Climate Sciences in Barcelona, Spain. However, it is not clear from the findings whether ozone causes Kawasaki disease, or whether ozone pollution could be a predictor of some other risk factor that is associated with high-ozone days, says Rodó, who was not involved in the Taiwan study. Ground-level ozone is created when nitrogen oxides and volatile organic compounds—found in vehicle exhaust, industrial emissions, and other sources—react in the presence of sunlight.[10]

The possibility of an airborne trigger is very plausible, says Burns. Children with Kawasaki disease develop enlarged lymph nodes under the jawbone but nowhere else in the body.

The origins of Kawasaki disease are still a mystery, although airborne agents appear likely to play a role. Researchers now report an association between hospitalizations for the disease and summertime exposures to ground-level ozone. © Anurak Pongpatimet/Shutterstock.

Those are the lymph nodes that drain the upper airway, she explains.

One possible direction for future studies is to compare Kawasaki cases in locations in different parts of the world and incorporate statistical models that can further investigate associations among several environmental factors. "Whether ozone holds up in other analyses in different parts of the world as a trigger or whether it is a marker for the real trigger," Burns says, "this is a productive avenue of research that deserves more focus."

Lindsey Konkel is a New Jersey–based journalist who reports on science, health, and the environment.

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